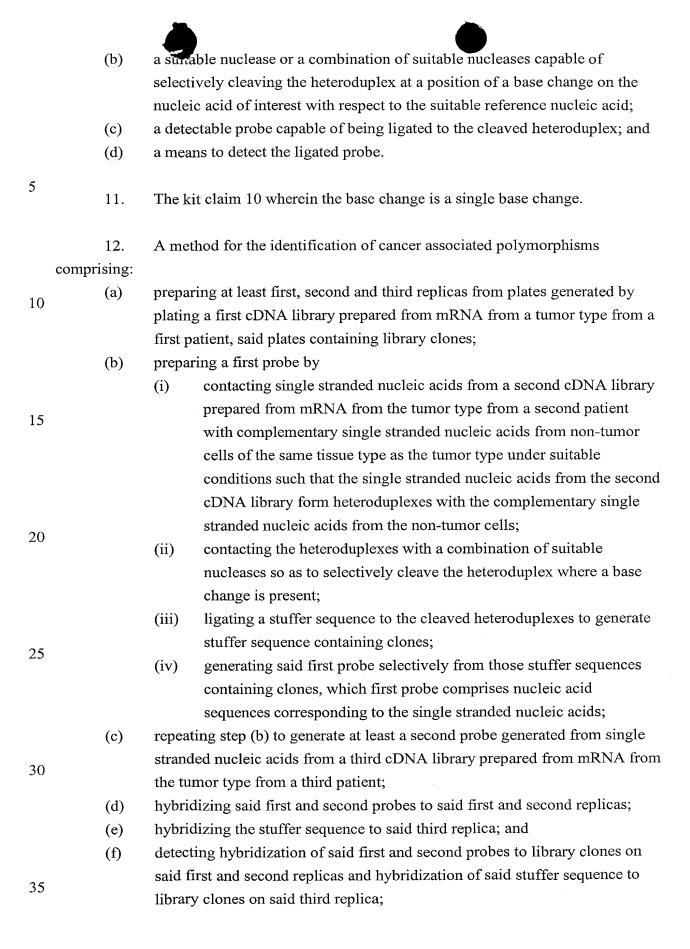


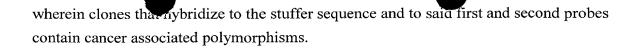
I CLAIM:

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- 1. A method for detecting base changes in a nucleic acid of interest which comprises the following steps:
 - (a) contacting the nucleic acid of interest with a suitable reference nucleic acid under suitable conditions such that the nucleic acid of interest forms a heteroduplex with the reference nucleic acid;
 - (b) contacting the heteroduplex with a suitable nuclease or a combination of suitable nucleases so as to selectively cleave the heteroduplex at a position of a base change on the nucleic acid of interest with respect to the reference nucleic acid;
- 10 (c) ligating a detectable probe to the cleaved heteroduplex; and
 - (d) detecting the ligated probe under suitable conditions so as determine the presence and location the base change.
 - 2. The method claim 1 wherein the base change is a single base change.
 - 3. The method claim 1 wherein the nucleic acid of interest is RNA.
 - 4. The method of claim 3 wherein the RNA is expressed from a cDNA library.
- 5. The method of claims 1 wherein the reference nucleic acid is DNA.
 - 6. The method of claims 1 wherein the reference nucleic acid is a circular nucleic acid.
- 7. The method of claim 6 wherein the suitable nuclease is S1 nuclease.
 - 8. The method of claim 6 wherein the combination of suitable nucleases is S1 nuclease and RNAase I.
- 9. The method of claim 1 wherein the detectable probe is a nucleic acid.
 - 10. A kit for detecting base changes in a nucleic acid of interest which comprises the following components:
- (a) a suitable reference nucleic acid capable of forming a heteroduplex with the nucleic acid of interest;





- 13. The method of claim 12 wherein said first and second probes are RNA probes.
- 5 14. The method of claim 12 which further comprises the steps of:
 - (g) preparing a fourth replica;
 - (h) preparing a third probe generated from mRNA from single stranded nucleic acids from a fourth cDNA library prepared from mRNA from the tumor type from a fourth patient;
- 10 (i) hybridizing said third probe to said fourth replica; and
 - (j) detecting hybridization of said third probe to library clones on said fourth replica;

wherein library clones that hybridize to the stuffer sequence and to said first, second and third probes contain cancer associated polymorphisms.

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